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STUDIES ON CONTACT INSECTICIDES.

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NATURE OF THE STUDY.

Contact insecticides are commonly understood to be substances which are capable of killing insects when dissolved or emulsified in liquid media or contained in dusts and brought into contact with their bodies. Fumigants, on the other hand, are substances which kill when applied in the gaseous condition. The distinctions are not sharp, as it is obvious that a volatile poison might kill by contact of the insect with either its liquid or its gaseous phase.

This investigation involves a study of the toxicity of the more readily available organic compounds when used as contact insecticides. In addition, a number of compounds which offered possible value as insecticides or which served to indicate working theories of insect toxicology were made in the laboratory. It is expected that this investigation will form the basis for future study and possibly lead to the discovery of compounds of commercial importance.

Most of the compounds tested showed little toxicity. These were ordinarily used in but few experiments unless questions of theoretical significance appeared to be involved. Those compounds which showed appreciable toxicity were subjected to greater study when available in sufficient quantity. Particular attention was given to the compounds which offered possible commercial value.

In addition to the data on the insecticidal value of the various compounds, information on the effect of the various chemicals on

[1] The writers are indebted to W. S. Abbott, entomologist of the Federal Insecticide and Fungicide Board's laboratory at Vienna, Va., for assistance with some of the experiments.

the plant is also included. The plant tolerance of a compound is considered to be the maximum concentration at which no appreciable destruction of plant tissue is caused. No special effort has been made to ascertain the exact plant tolerance for each compound, and the values given are usually less accurate than those obtained for the insect.

PROCEDURE.

The black aphis, infesting nasturtium (*Tropaeolum majus*) and many other plants, was used exclusively in these experiments. It was identified as *Aphis rumicis* L. by Dr. A. C. Baker, of the Bureau of Entomology.[2] This species is easily reared on nasturtium plants in the greenhouse at all times of the year except the hottest parts of the summer, when reproduction appears to be retarded. In the present study it has been found much less frequently attacked by hymenopterous parasites than the other species reared in the greenhouse. Furthermore, this aphis has a tendency to remain on the plants even when sprayed with toxic or irritating substances, a habit of considerable convenience to the experimenter.

Dwarf nasturtium plants (*Tropaeolum majus*) grown in small flowerpots were used as food plants for the aphids. This plant seems to be relatively sensitive to chemicals, and it is probable that concentrations of many compounds which will kill nasturtium would be harmless to the foliage of orchard trees.

The compounds were prepared for application in a number of ways. Immiscible liquids were applied as emulsions, fish-oil soap, capryl alcohol, and in a few instances amyl alcohol being the emulsifying agents. Liquids soluble in water were mixed with a small amount of fish-oil soap to enable the solution to wet and spread over the foliage. If the liquids were basic or acidic compounds they were applied as soluble salts; the basic compounds were converted to sulphates or chlorides and the acid compounds to their ammonium salts. The solids tested were either soluble as such in water or were made so by conversion to the salt form, as stated for the liquids. A spreader, usually fish-oil soap, when applicable, was also used with these solutions.

The solutions or emulsions were sprayed on the plants by means of a small hand atomizer. Usually a pot containing several plants well infested with aphids was used for each test. In some experiments a portion of a plant was placed in a bottle containing water and sprayed, care being taken to see that the stem was surrounded by cotton to prevent the dead insects from falling in. An untreated plant, immersed in water in this fashion, will support a colony of aphids in a normal condition for several days. Eighteen or 24 hours after spraying the percentage of aphids killed was determined and the condition of the plants noted.

The toxic concentration was arbitrarily considered to be the minimum capable of killing about 95 per cent of the aphids, or, to state it in a different way, it represents the concentration which leaves an average of 5 per cent alive. In many instances this figure was

[2] According to Doctor Baker there is still some confusion regarding the number of species of aphids included under the name *rumicis*. He states, however, that the black aphis found on our plants belongs to a single species, whatever that may ultimately prove to be. The name *rumicis* is therefore tentatively applied to the aphis used in these experiments.

not ascertained because of lack of material; in others its importance did not seem to justify the expenditure of time.

Many factors combine to influence the accuracy of experiments of this nature. Some compounds partially annul the spreading and wetting effect of the fish-oil soap or capryl alcohol. There is also a tendency for the liquid to collect in drops or thick layers on the lower edges of the leaves and stems, and, as the water or compound evaporates, subject the aphids in those places to a different concentration of the chemical than on other parts of the plants. Furthermore, young aphids are more susceptible to most chemicals than the older ones, so that the ratio of young to mature has a bearing on the number which will be killed by a given concentration of a compound. It has usually been observed also that high humidity or low temperature favors toxicity, presumably because of lessened evaporation. All of these experiments have been made in a greenhouse where the influence of the above factors has been partially overcome by repetition and by making the tests only during bright weather. No doubt they will give a fairly accurate idea of the relative toxicity of the different compounds to *Aphis rumicis*.

In Table 1 are assembled the results of the study. The concentrations are given in grams per 100 cubic centimeters of solution or emulsion. For comparison, the concentrations in Table 2 are figured also in gram molecules per liter. Fish-oil soap was almost invariably used in the proportion of 0.3 gram of moisture-free soap per 100 cubic centimeters, and capryl alcohol at 0.2 to 0.3 cubic centimeter per 100 cubic centimeters. Blank experiments showed little killing at these concentrations. The classification adopted for the compounds is only for convenience.

DETAILED RESULTS OF EXPERIMENTS.

TABLE 1.—*Results of spraying Aphis rumicis with organic compounds.*

PYRIDINE, QUINOLINE, AND ALLIED COMPOUNDS.

Compound.	Concentrations tested.	Minimum toxic concentrations.	Tolerance of plant.
	Grams per 100 cc.	*Grams per 100 cc.*	*Grams per 100 cc.*
Pyridine	(1)	25	25–30
Pyridinium ethyl iodide	1 0.8 0.5 0.1 0.05	>1	0.8–1.0
Pyridinium ethyl hydroxide	0.5 0.1	>0.5	<0.5
Piperidine	(1)	5.0	0.5–1.0
Piperidine sulphate	(1)	0.94	0.8
Chloropiperidine (crude)	0.5 0.1 0.05	>0.5	>0.5
n-Ethyl piperidine	0.5 0.1 0.05	>0.5	>0.5
n-Ethyl piperidine sulphate	1.86 0.93 0.46	±0.93	<0.46
Methylene dipiperidine	1 0.5 0.1	>1.0	0.5–1.0
γ, γ-Dipyridyl	(1)	>1.0 [2]	<0.25
α-Picoline	25 20 15 10	±15	10–15
Pyrrole	2 1 2	>2	>2
Quinoline	(1)	2.0	<0.5
Tetrahydroquinoline	(1)	2.0	<0.4
Quinaldine	1 0.2	>1.0	<1.0
4-Dimethylaminoantipyrine [3]	0.5	>0.5	<0.5
Nicotinic acid nitrate	0.8 0.4 0.1	>0.8	<0.1
Piperazine	(1)	3.5	2

ALKALOIDS.

Quinine (applied as hydrochloride) [3]	1 0.2	>1 [4]	>1 [4]
Cocaine (applied as hydrochloride) [3]	1 0.2	>1 [4]	<1 [4]?
Hyoscyamine (applied as sulphate) [3]	0.4	>0.4 [4]	>0.4 [4]
Pilocarpine hydrochloride [3]	0.5	>0.5	>0.5
Aconitine (applied as sulphate) [3]	0.5	>0.5 [4]	>0.5 [4]
Coniine hydrochloride	0.5 0.12 0.06	>0.5	>0.5
Codeine sulphate	0.5 0.12	>0.5	>0.5
Brucine (applied as sulphate) [5]	0.5 0.12	>0.5 [4]	>0.5 [4]
Narcotine (applied as sulphate) [5]	0.5	>0.5 [4]	>0.5 [4]
Strychnine sulphate [3]	0.5	>0.5	>0.5
Cinchonine (applied as sulphate) [3]	0.5	>0.5 [4]	>0.5 [4]
Cinchonidine (applied as sulphate) [3]	0.5	>0.5 [4]	<0.5 [4]?
Quinidine (applied as sulphate) [3]	0.5	>0.5 [4]	>0.5 [4]
Curare	0.5	>0.5	>0.5
Caffeine	0.5	>0.5	>0.5
Nicotine	(1)	0.007	>0.05
Nicotine sulphate	(1)	0.009	>0.013
Atropine sulphate	(1)	5	1–2
Hexahydronicotine	(1)	0.6	0.5–0.6

[1] Many concentrations tested. [2] Capryl alcohol used as spreader. [5] 1 per cent amyl alcohol spreader.
[3] Saturated solution. [4] Figures refer to free base.

TABLE 1.—*Results of spraying Aphis rumicis with organic compounds*—Continued.

AMINES, AMIDES, IMIDES, ORGANIC AMMONIUM COMPOUNDS, ETC.

Compound.	Concentrations tested.	Minimum toxic concentrations.	Tolerance of plant.
	Grams per 100 cc.	*Grams per 100 cc.*	*Grams per 100 cc.*
Methylamine hydrochloride	(1)	3	0.3–0.5
Trimethylamine hydrochloride	(1)	0.5	0.4
Tetramethylammonium chloride	(1)	0.35	0.3–0.5
Diethylamine	2	>2	<2
Triethylamine	(2)	>15	?
Triethylamine hydrochloride [7]	(1)	3	<1
Tetraethylammonium chloride	(1)	3.5	0.1–0.3
Tetrapropylammonium hydroxide	(1)	3	<0.1
Isobutylamine	1	>1	<1
Diamylamine	1	±1	<1
Triacetonamine (crude)	1	>1	<1
Hexamethylenetetramine	10 7 5	7–10	?
Formamide	1	>1	>1
Dicyandiamide	1	>1	>1
Choline hydrochloride	1	>1	<1
Betaine hydrochloride	1	>1	<1
Nitroguanidine	1	>1	>1
Succinimide	1 0.5	>1	0.5–1
Aniline	(1)	15	<1
Benzylamine	(1)	3	1
Benzidine hydrochloride [8]	1	>1	<1
Metaphenylenediamine hydrochloride	1	>1	<1
Paraphenylenediamine	0.5 0.1	>0.5	0.1–0.5
Phthalimidine	0.5 0.1	>0.5	0.1–0.5
Camphylamine	1 0.5	>1	<0.5
Tetrahydro-beta-naphthylamine hydrochloride	1 0.5	>1	±0.5

ALDEHYDES, KETONES, AND ALLIED COMPOUNDS.

Paraldehyde	(1)	28	<10
Aldehyde ammonia	10 7.5 5 4 2	>10	?
Acetal	50 75 Pure liquid.	50–75	<50
Chloral hydrate	10 7.5 5.0 2.5	>10	<2.5
Furfural	(1)	>32	?
Benzaldehyde	(1)	5	1–4
Acetone	(1)	(9)	50–75
Methyl-ethyl ketone	(1)	(9)	20–30

ALCOHOLS.

Methyl alcohol	(1)	(9)	(9)
Ethyl alcohol	(1)	(9)	67–70
n-Propyl alcohol	(1)	50	50
n-Butyl alcohol	(1)	35	<30
Capryl alcohol	(1)	5	<3
Iso-amyl alcohol	(1)	±10	±10
Benzyl alcohol	(1)	5	<2
Furfuryl alcohol	20 2 1	>20	2–20

[1] Many concentrations tested.
[2] Capryl alcohol used as spreader.
[3] Many concentrations tested up to 15 grams per 100 cubic centimeters.
[7] Capryl alcohol as spreader in some experiments, soap in others.
[8] Pure liquid killed less than 95 per cent.
[9] Pure liquid produced slight burn.

TABLE 1.—*Results of spraying Aphis rumicis with organic compounds*—Continued.

PHENOLS AND ALLIED COMPOUNDS.

Compound.	Concentrations tested.	Minimum toxic concentrations.	Tolerance of plant.
	Grams per 100 cc.	*Grams per 100 cc.*	*Grams per 100 cc.*
Phenol	(1)	5.5	<2
Cresol (U. S. P.)	(1)	1.5	0.1–0.5
Resorcinol	(1)	5.5	<3
Phloroglucinol	1	>1	>1
Pyrogallol	(1)	15	<1
Cyclohexanol	1	>1	>1
Terpineol	1	>1	<1
Safrol	1	>1	<1
Sodium dioxynitrosobenzene	1	>1	<1

ESTERS.

Amyl acetate (commercial)	(1)	>12	<2.5
Methyl salicylate	(1)	5	<1
Benzyl acetate	1	>1	<1
Benzyl chloride	(1)	5	1

ORGANIC ACIDS AND THEIR SALTS.

Cyanacetic acid (applied as the ammonium salt)	1	>1 [10]	<1 [10]
α–Naphthol, 1, 3, 6, 8-trisulphonic acid	1	>1	<1
α–Naphthol disulphonic acid 1,3,6	1	>1	<1
1, 8-aminonaphthol, 3, 6-disulphonic acid [2]	1	>1	>1
Sodium β–Naphthol sulphonic acid 2,6	1	>1	>1
Sodium β–Naphthol disulphonic acid 2,6,8	1	>1	>1
Sodium naphthionate	1	>1	>1
Camphoric acid (applied as the ammonium salt)	1	>1 [10]	<1 [10]
Sodium phenol sulphonate (U. S. P.)	6 8 10 Sat. soln.	Sat. soln. (20±)	8–10
Cyanuric acid (applied as the ammonium salt)	0.5	>0.5 [10]	>0.5 [10]
Cacodylic acid [2]	1 0.1	>1	<0.1
Sodium salicylate	1 0.5	>1	<0.5
Sodium benzoate	1 0.5	>1	<0.5
Picric acid	1 0.5 0.1	0.5–1	<0.1
Fish-oil soap (Na base)	(1)	±6	3

CYCLIC COMPOUNDS WITH C AND H ONLY PRESENT.

Benzene	(1)	25	<5
Toluene	(1)	16	<4
Xylene (mixture of isomers)	(1)	10	<6
Cyclohexane	(1)	12.5	±2.5

ALIPHATIC AND CARBOCYCLIC COMPOUNDS WITH C AND H AND Cl OR S PRESENT.

Chloroform	(1)	34	2–5
Carbon tetrachloride	(1)	31	<8
Carbon disulphide	5 2	>5	<2
Chlorobenzene	(1)	9	<3
Trichlorobenzene (commercial)	(1)	6	<4

[1] Many concentrations tested. [2] Capryl alcohol used as spreader. [10] Figures refer to free acid.

TABLE 1.—*Results of spraying Aphis rumicis with organic compounds*—Continued.

ESSENTIAL AND FIXED OILS.

Compound.	Concentrations tested.	Minimum toxic concentrations.	Tolerance of plant.
	Grams per 100 cc.	*Grams per 100 cc.*	*Grams per 100 cc.*
Turpentine spirits (technical)	5 2.5 1 0.5 0.1	>5	1
Terebene (U. S. P.)	2 1 0.5 [11]	±2	<0.5
Pine oil	1	>1	<1
Oil cedar wood	1 0.5 0.1	±1	±0.5
Cottonseed oil	5 2.5 1.25 1	±2.5	<1

[11] By volume.

DISCUSSION OF TABLE 1.

The literature contains many references to the use of commercial and pure pyridine as an insecticide. As early as 1911, McClintock, Hamilton, and Lowe (*4*)[3] pronounced it valueless as a contact insecticide, and in the same year Cazeneuve (*2*) reported it as effective against Cochylis and Eudemis larvæ. More recently Theobald (*14*) has claimed great value for it as a substitute for nicotine in the control of apple aphids. Frayer (Insect Pests and Fungus Diseases, Cambridge, Eng., 1920, p. 445) has made a large number of tests with pyridine, but finds it a weak insecticide, injurious to foliage when used at the strength required to kill aphids or capsids. Results of the present study indicate that carefully purified pyridine, boiling at 115° C., shows little toxicity for *Aphis rumicis*. Alpha picoline, the next homolog, proved to be more toxic, killing at about 15 per cent. Experiments not included in this table indicate that the higher boiling fractions of the commercial product up to 160° C. have somewhat higher toxicity, though they offer little promise as contact insecticides. Quaternary pyridinium compounds gave little toxicity. Piperidine (hexahydropyridine) is to be noted as having five times the effectiveness of pure pyridine. When used as a sulphate, the toxicity was several times greater than that of the free base. This important difference is discussed on page 10. Quinoline is much more toxic than pyridine, killing at 2 per cent. Tetrahydroquinoline is equally toxic. The insecticidal effect of piperazine is slightly greater than that of piperidine, the chemical structure of which is very similar. Pyrrole produced little effect at the concentrations used. Pyridine, alpha picoline, and their homologs as found in commercial pyridine, are relatively noninjurious to nasturtium; most of the other compounds in this series are decidedly injurious.

Alkaloids, with the exception of nicotine, showed little toxicity. Nicotine, however, is toxic at a concentration of 0.007 per cent, the

[3] Reference is made by number (italics) to Literature cited, p. 15.

lowest for the compounds used in this study. The reduction of nicotine to hexahydronicotine results in greatly lowered toxicity. The hydrochloride of coniine (alpha n-propyl piperidine) is probably toxic at approximately 1 per cent. Atropine sulphate, because of its large molecule, gives a lower molar toxic concentration than its concentration in grams per 100 cubic centimeters would suggest.

The outstanding results for the group containing amines, amides, and similar compounds are the pronounced toxicities of certain methylamine, ethylamine, and alkyl ammonium compounds. The methylamine compounds are more toxic than the corresponding ethylamines. It is to be further noted that of the methyl derivatives, the trimethyl and tetramethyl are most effective. The increased toxicity of benzylamine as compared with aniline is interesting. The plant tolerance for these compounds is generally low.

The aldehydes and ketones, with the exception of benzaldehyde, are practically without effect on either insect or plant.

With the exception of capryl alcohol, the aliphatic alcohols have little toxic value. Benzyl alcohol, a cyclic compound, is moderately toxic.

U. S. P. cresol is more toxic than phenol and resorcinol. Pyrogallol shows little toxicity.

The esters showed some toxicity to the insect and were harmful to the plant.

The various sulphonic acids and their salts showed no appreciable toxicity to the aphids. Attention should be directed to the decreased toxicity of sodium phenol sulphonate (U. S. P.) as compared with phenol. Picric acid showed appreciable toxicity, but was quite injurious to the plant. The minimum toxic concentration of the fish-oil soap used in most of these experiments was about 6 grams per 100 cubic centimeters; at 0.3 gram per 100 cubic centimeters, the concentration used in these experiments, it killed an average of 14 per cent.[4]

The slight toxicity of the benzene series was found to increase from benzene through toluene to xylene. The plant tolerance, however, is low.

Chloroform and carbon tetrachloride require about 30 grams per 100 cubic centimeters for the lethal concentration. Plant tolerance was small. The substitution of chlorine into the benzene ring was found to increase toxicity.

The essential and fixed oils showed some toxicity to both insect and plant.

[4] This figure has not been deducted from the toxicity values given in this paper. Since relative values are most important in an investigation of this nature, and, further, since 0.3 per cent fish-oil soap was used in most of these experiments, the deduction of the comparatively small soap toxicity is not considered essential.

TOXIC CONCENTRATIONS OF SELECTED COMPOUNDS.

TABLE 2.—*Relative toxicity of selected compounds to Aphis rumicis.*

Compound.	Toxic concentration.		Boiling point.
	Gram molecules per liter.	Grams per 100 cubic centimeters.	
			°C.
Nicotine	0.0004	0.007	247
Nicotine sulphate	.0002	.009	----
Tetramethylammonium chloride	.032	.35	----
Piperidine sulphate	.035	.94	----
Hexahydronicotine	.036	.60	246
Trimethylamine hydrochloride	.052	.50	----
Atropine sulphate	.074	5	----
Cresol (U. S. P.)	.14	1.5	195–205
Quinoline	.15	2.0	238
Tetrahydroquinoline	.15	2.0	246–250
Tetrapropylammonium hydroxide	.15	3.0	----
Tetraethylammonium chloride	.21	3.5	----
Triethylamine hydrochloride	.22	3	----
Benzylamine	.28	3	185
Methyl salicylate	.33	5	222
Trichlorobenzene	.33	6	208–218
Capryl alcohol	.38	5	174–185
Benzyl chloride	.39	5	179
Piperazine	.41	3.5	145
Methylamine hydrochloride	.44	3	----
Benzyl alcohol	.46	5	206
Benzaldehyde	.47	5	180
Resorcinol	.50	5.5	280
Phenol	.58	5.5	183
Piperidine	.59	5	106
Chlorobenzene	.80	9	132
Xylene (mixed isomers)	.94	10	136–141
Pyrogallol	1.2	15	293
Cyclohexane	1.5	12.5	81
Aniline	1.6	15	184
Toluene	1.7	16	111
Carbon tetrachloride	2.0	31	77
Paraldehyde	2.1	28	124
Chloroform	2.8	34	61
Benzene	3.2	25	80
Pyridine	3.2	25	115
n-Butyl alcohol	4.7	35	117
n-Propyl alcohol	8.3	50	97
Methyl alcohol	(1)	(1)	66
Ethyl alcohol	(1)	(1)	78
Acetone	(1)	(1)	57
Methyl-ethyl ketone	(1)	(1)	80

[1] Pure liquid kills less than 95 per cent.

DISCUSSION OF TABLE 2.

The compounds which have received the most attention are grouped in Table 2. These are arranged in the order of their toxicities on the basis of concentration expressed in gram molecules per liter. Their toxicities in grams per 100 cubic centimeters, together with their respective boiling points, are also included. The nitrogen-containing compounds, in general, are found to be grouped at the head of the series. In the middle portion of the series (molar concentrations between 0.33 and 1.7) the cyclic derivatives predominate and of these three contain nitrogen. Two aliphatic compounds appear, one of which contains nitrogen. The remaining compounds of lowest toxicity are aliphatic with the exceptions of benzene and pyridine. Pure liquid methyl and ethyl alcohol, acetone, and methyl-ethyl ketone killed less than 95 per cent of the aphids.

TOXICITY OF CERTAIN BASES COMPARED WITH THEIR SALTS.

Results are given in the preceding tables which show differences in toxicity between certain bases and their salts. The toxic concentration for piperidine sulphate was found to be 0.035 moles (equal to 0.070 moles of the free base per liter) while that for piperidine base was 0.59 moles, or an amount about eight times greater. Triethylamine base requires more than 1.5 moles, while its hydrochloride requires only 0.22, a ratio of at least 7 to 1. A comparison of nicotine and nicotine sulphate was also made. A definite quantity of nicotine sulphate was prepared by titrating the free base with normal sulphuric acid, using methyl red as indicator and diluting to the desired strength. In this instance no difference in toxicity was observed, but exception can rightly be taken to a comparison of nicotine with nicotine sulphate in such small concentrations when 0.3 per cent fish-oil soap is used in the solution. Nicotine is a weak base whose salts hydrolyze slightly in dilute solution and furthermore are decomposed by the free alkali of the hydrolyzed soap. These considerations do not apply to the conclusions reached with the salts of piperidine and triethylamine, for the latter compounds are salts of strong bases and much larger concentrations of them were used in relation to the soap present. Further study is being given to this subject and it will not be discussed at greater length here.

TOXICITY AND VOLATILITY.

The data obtained from these toxicity studies are of interest in another connection. The work of Moore and coworkers (*5, 6, 7, 10, 12*) indicates that the toxicity of volatile organic compounds when employed in the vapor state against insects or applied directly to the surface of insects' eggs varies with the volatility. Up to a boiling point of 225–250° C., toxicity, it is asserted, increases as the boiling point rises and the volatility decreases. Compounds with higher boiling points generally have such low volatility that their vapor concentrations are not great enough to kill within a reasonable time. Other studies by Moore, and Moore and Graham (*8, 9, 11*) with contact insecticides led to the conclusion that "volatility is an index of the ability of the compound to gain entrance into the insect and is therefore closely correlated with toxicity." It was further stated that compounds more volatile than xylene evaporate too quickly to be effective.

While the results of the present study show that, in general, the most toxic compounds employed were among the least volatile and the least toxic compounds were the more volatile ones, there are so many exceptions that the writers believe neither volatility nor the boiling point can be used as a safe index of toxicity when the compound is employed as a contact insecticide. For example, quinoline with a boiling point close to that of nicotine has, in these experiments, only about one-three hundred seventy-fifth the toxicity of the latter. On the other hand, tetramethylammonium chloride, a nonvolatile salt at ordinary temperatures, is one of the most toxic substances tested. The tetraethyl- and tetrapropylammonium compounds are also nonvolatile, yet they show considerable toxicity. Benzylamine and aniline have closely similar boiling points but differ widely in toxicity; and this is also true of cyclohexane and benzene. Piperidine with a

boiling point of 106° C. is considerably more toxic than the nearly related pyridine, which has a boiling point of 115° C. Paraldehyde with a boiling point of 124° C. has only about one-third the toxicity of chlorobenzene, whose boiling point is but 8° higher. Pyrogallol, aniline, and toluene have closely similar toxicities, but widely divergent boiling points. A study of Table 2 will reveal other discrepancies. Tattersfield and Roberts (*13*), in a recent study of the effects of vapors of organic compounds on wireworms, conclude that while "there is a fairly close relationship between toxicities and the vapor pressures, rates of evaporation, and volatilities of compounds of the same general type," lethal effects are often directly determined by chemical constitution. Compounds with irritating vapors, such as allyl isothiocyanate, chloropicrin, and benzyl chloride, gave toxic values which were not closely correlated with their vapor pressures or rates of evaporation. It was also found that isomeric compounds having similar boiling points sometimes differ widely in toxicity.

There can be no question of the importance of volatility as a factor in the toxicity of both contact insecticides and fumigants. But the toxicity of a chemical appears frequently to depend upon properties other than volatility. High toxicity, therefore, may occur in compounds like chloropicrin and hydrogen cyanide, which have high volatility, or in nicotine and tetramethylammonium chloride, in which the volatility is low or almost nil.

TOXICITY AND CHEMICAL STRUCTURE.

The addition of hydrogen atoms to the cyclic nucleus has a marked effect on the toxic activity of some compounds. Piperidine (hexahydropyridine) has about five times the toxic activity of pyridine. Cyclohexane (hexahydrobenzene) is more toxic than benzene, but the increase is not so marked as that observed for piperidine. On the other hand, quinoline and tetrahydroquinoline are of approximately equal toxicity. Hydrogenation of the pyridine nucleus of nicotine to form hexahydronicotine greatly reduces toxicity, the lethal concentration for hexahydronicotine being about ninety times that of nicotine. The addition of hydrogen atoms to the ring, therefore, may either increase or decrease toxicity. It should also be noted that although the changes in toxicity resulting from the addition of hydrogen may be considerable, the differences in boiling point between parent and hydrogenated compound are small.

In a number of instances it was noted that the toxicity of homologous compounds increased as the series ascended. This is particularly well shown in the series, benzene, toluene, xylene, and in the aliphatic alcohols, methyl, ethyl, normal propyl, normal butyl. The phenol series, phenol, resorcinol, pyrogallol, does not show this relation, pyrogallol having only about one-half the toxicity of resorcinol. This is contrary to what has been observed in higher animals, in which an increase in the number of OH groups in the benzene ring is generally accompanied by increased toxicity (*1, p. 29*). The trimethylamine and triethylamine hydrochlorides and the tetramethylammonium and tetraethylammonium chlorides are also exceptions, for in each case the lower members (methyl compounds) are the most toxic. Tattersfield and Roberts (*13*) have also recorded increased toxicity in successive members of homologous series of

compounds when used as fumigants, but state that at a certain point in the series the toxicity becomes uncertain because of the small amount of the compound which enters the gaseous phase owing to the low vapor pressure. This is certainly not true of the aliphatic substituted ammonium salts mentioned above when used as contact insecticides, since they are practically nonvolatile and at the same time quite toxic.

Tattersfield and Roberts indicate that the effect of substitution of various atoms and groups into a compound depends upon the nature of the parent compound and the group or atom introduced. Some of the writers' results are in harmony with theirs. Thus they found that each CH_3 introduced into benzene approximately doubled the toxicity of the substituted compound. Table 2 shows that benzene was toxic at 3.2 moles per liter, toluene ($C_6H_5CH_3$) at 1.7, and xylene ($C_6H_4(CH_3)_2$) at 0.94, or nearly double the toxicity for each CH_3 group introduced. Moore (*5*) found benzene to be slightly more toxic than toluene in the gaseous phase against house flies (*Musca domestica* L.). Xylene, however, was more toxic than either. The chlorine atom, on the other hand, was found by Tattersfield and Roberts to increase the toxicity of the substituted benzene compounds from three to four times for each substitution. A similar result was obtained by us with chlorobenzene, the molar toxicity of which was 0.80, or four times that of benzene. Commercial trichlorobenzene was more toxic than chlorobenzene, but not in the same ratio. It was possibly a mixture of several isomers. Previous work by Moore (*5*) shows that the introduction of halogen into the benzene ring increases toxicity, iodine being the most effective, chlorine the least, and bromine having an intermediate value. The writers' experiments show a greater toxicity when OH is introduced into toluene to form cresol than when introduced into benzene to form phenol, a result which is the reverse of that recorded by Tattersfield and Roberts for wireworms.

Introduction of NH_2, OH, or Cl in the side chain (CH_3 group) of toluene gave interesting results. Benzylamine is the most toxic, and benzyl alcohol the least, when the molar toxicities are compared. All are considerably more toxic than the parent compound, toluene. The experiments of Tattersfield and Roberts indicate that benzyl chloride in the vapor phase is highly toxic to wireworms.

Moore (*5*) has pointed out the increased toxicity resulting from the introduction of the CHO group into benzene, and results obtained in the present study with benzaldehyde as a contact insecticide against *Aphis rumicis* indicate a similar relationship.

Tattersfield and Roberts observed considerable toxicity among the aliphatic amino compounds which they tested. Methylamine, dimethylamine, and ethylamine were about as effective as fumigants for wireworms as hydrocyanic acid and ammonia; trimethylamine was slightly less poisonous. They were far more toxic than pyridine, and somewhat more toxic than aniline. Their toxicities did not in any sense correspond with their extremely high volatilities. It was suggested that their solubilities, the readiness with which they are absorbed, and their ability to ionize may account for the relatively high toxicities of these compounds. The writers have observed high toxicity among certain aliphatic amines and related compounds. If the results with triethylamine may be taken as representative, the salts of these amines are more effective than the corresponding bases.

The present experiments indicate that trimethylamine hydrochloride is much more effective than methylamine hydrochloride, the reverse of what Tattersfield and Roberts found with the corresponding bases when used as fumigants.

GENERAL DISCUSSION.

In the present state of knowledge of insecticides, it is doubtful whether one may safely draw any far-reaching conclusions as to the relation between the physical properties of compounds and their toxicity. Any large and varied series of toxic compounds will show differences in toxicity which can not be correlated with molecular weight, volatility, solubility, ionization, permeability, or other properties.

Neither can these differences always be harmonized with differences in chemical structure. Many powerful poisons like nicotine and coniine contain nitrogen; others like "pyrethron,"[5] which, in crude form (contaminated with plant extractives), was found to be slightly more toxic to *Aphis rumicis* than nicotine, contain no nitrogen. The saturation of a cyclic compound with hydrogen may either increase or reduce toxicity, as has been pointed out in the case of piperidine and hexahydronicotine. The introduction of chlorine into benzene compounds seems usually to increase toxic activity, but its effectiveness varies greatly with the nature of the other groups present.

Other instances could be mentioned, but these will suffice to illustrate the point. Indeed, the more these facts are studied, the more it seems probable that pharmacological action in insects is, in many respects, fundamentally like that in higher animals, and that the statement of Cushny (*3, p. 20*) can be accepted when he says: "From the present confusion the only legitimate conclusion seems to be that the activity of drugs depends on a large variety of factors and that pharmacological action can not be brought under any one law, either chemical or physical."

In this investigation the writers have chosen chemical structure as the best basis for comparison; that is, so far as obtainable, those compounds have been selected which are chemically allied to others of known toxicity. While this method has brought many failures, it has led to the discovery of apparently new compounds of high toxicity which may properly be the subject of another paper.

CONCLUSIONS.

This is a report of a laboratory study on the effect of a number of organic compounds as contact insecticides for *Aphis rumicis* L. living on nasturtium plants.

Pyridine, alpha picoline, and commercial pyridine containing the higher homologs of pyridine were of little value as contact insecticides.

The alkaloids, with the exception of nicotine, were of low toxicity. Nicotine, however, was the most toxic compound investigated (excluding "pyrethron").

[5] A series of tests were made with crude "pyrethron," but these were not extensive enough to include in the tables.

The aliphatic amines and substituted ammonium compounds showed considerable toxicity. Tetramethylammonium chloride was the most toxic, methylamine hydrochloride the least. Of the two cyclic amines, benzylamine was five times as toxic as aniline.

The aliphatic aldehydes and ketones had a low order of toxicity. Benzaldehyde was moderately toxic.

The aliphatic alcohols showed little toxicity. Benzyl alcohol, a cyclic compound, was more toxic.

Cresol U. S. P. was the most toxic of the phenols, pyrogallol the least, while phenol and resorcinol occupied an intermediate position.

The esters of cyclic compounds showed some toxicity.

Sulphonic acids and their salts had little effect. Picric acid and sodium salicylate showed appreciable toxicity. Fish-oil soap (sodium base) was relatively ineffective.

Benzene, toluene, and xylene were only slightly toxic.

Aliphatic compounds containing chlorine were but slightly toxic; benzene derivatives containing chlorine were much more toxic.

Essential and fixed oils showed some toxicity.

Piperidine as the sulphate and trimethylamine as the hydrochloride when applied in dilute soap solution were more toxic than the respective free bases. Nicotine as the sulphate and nicotine base were of approximately equal toxicity.

Pyridine and its homologs as found in commercial pyridine, alkaloids, sodium phenol sulphonate U. S. P., aliphatic aldehydes and ketones and aliphatic alcohols of low molecular weight were relatively nontoxic to the nasturtium plant. Most of the other compounds used in this investigation had considerable toxicity.

Neither the volatility nor the boiling point is a reliable index of the toxicity of organic compounds when used as contact insecticides.

Chemical structure does not appear to be a dependable index of toxicity. Nevertheless, it is probably the best empirical guide at present available for the study of contact insecticides.

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